



## Epizyme's EPZ-5676 DOT1L Inhibitor Demonstrates Encouraging Initial Findings in an Ongoing Phase 1 Dose Escalation Study

- **Four dose cohorts (12, 24, 36 and 54 mg/m<sup>2</sup>/day) completed (16 patients, 8 with acute leukemia with MLL-r) with 21-day on/7-day off administration schedule**
- **Observations to date include:**
  - No dose-limiting toxicities; maximum tolerated dose (MTD) not reached
  - Treatment effects, consistent with genetically defined therapeutic mechanism of action, observed in 4 of 8 acute leukemia patients with MLL-rearrangement (MLL-r); no effects observed in non-MLL-r patients
  - Dose-proportional exposure
  - Dose- and time-dependent methyl mark inhibition
- **Plan to initiate Phase 1 MLL-r only expansion stage in December 2013 starting at an 80 mg/m<sup>2</sup>/day uninterrupted treatment schedule, continued dose escalation possible**
- **Epizyme will host a conference call and live audio webcast today at 8:30 a.m. ET to discuss these data; slides will be available on [www.epizyme.com](http://www.epizyme.com) prior to call**

Cambridge, Mass. – November 14, 2013 – [Epizyme, Inc.](http://www.epizyme.com) (NASDAQ: EPZM), a clinical stage biopharmaceutical company creating innovative personalized therapeutics for patients with genetically defined cancers, today announced initial findings from an ongoing Phase 1 study of EPZ-5676, a potent and selective inhibitor of the DOT1L histone methyltransferase (HMT) being developed for the treatment of acute leukemia with alterations in the *MLL* gene.

"EPZ-5676 is a first-in-class inhibitor of the DOT1L HMT, and we are very pleased with the findings to date in the dose escalation stage of the ongoing two-stage Phase 1 study," said Robert J. Gould, Ph.D., chief executive officer, Epizyme. "The safety, pharmacokinetic, pharmacodynamic, and treatment effects observed in this study are consistent with our pre-clinical data. Based on these results, we plan to initiate the MLL-r only Phase 1 expansion stage in December 2013 and pediatric MLL-r and MLL-PTD studies in early 2014."

The dose escalation stage of the Phase 1 study, evaluating a 21-day on/7-day off administration schedule, is open to patients with heavily pre-treated advanced hematological malignancies, including but not limited to patients with acute leukemia with MLL-rearrangements (MLL-r). Study objectives are typical for a Phase 1 study, including determining safety and tolerability, identifying the maximum tolerated dose or recommended Phase 2 dose (RP2D) and schedule, and evaluating the relationship between dose, exposure and pharmacodynamic effects. In four completed dose cohorts, with a total of 16 patients dosed (including eight patients with acute leukemia with MLL-r), EPZ-5676 has been well-tolerated. There have been no dose-limiting toxicities and only one adverse event-related

treatment discontinuation, which was not considered to be related to EPZ-5676. Exposure has been dose-proportional, and inhibition of the target methyl mark has been dose- and time-dependent. In four of the eight MLL-r acute leukemia patients, treatment effects consistent with the genetically defined therapeutic mechanism of action were observed, while no treatment effects were seen in the non-MLL-r patients. Treatment effects were consistent with leukemia cell differentiation and maturation, including treatment-related leukocytosis, maturation features in blood and bone marrow, and blood and bone marrow blast count reductions. Additionally, some MLL-r patients experienced resolution of leukemia-related symptoms and manifestations, including fevers, cachexia, and leukemia cutis. The study is ongoing with a fifth dose cohort (80 mg/m<sup>2</sup>/day) currently enrolling.

Based on these results, Epizyme plans to start the Phase 1 MLL-r only expansion stage with an 80 mg/m<sup>2</sup>/day administration schedule without a drug holiday and with possible continued dose escalation. This expansion stage is intended to provide an initial assessment of efficacy for EPZ-5676 in MLL-r patients.

"The observed safety and tolerability profile of EPZ-5676, along with the mechanistically consistent treatment effects in MLL-r patients, are strongly supportive of continued clinical development," said Eric Hedrick M.D., chief medical officer, Epizyme. "We believe these data warrant evaluation of an uninterrupted administration schedule of EPZ-5676 in the MLL-r only expansion stage of the ongoing Phase 1 adult trial, as well as in two additional clinical settings, both of which we plan to initiate in 2014: a Phase 1b trial in pediatric acute leukemia patients with MLL-r, and an expansion cohort in adult AML patients with the MLL-PTD genetic alteration."

#### **About EPZ-5676**

Epizyme is developing EPZ-5676, a small molecule inhibitor of DOT1L created with Epizyme's proprietary product platform, for the treatment of acute leukemias with alterations in the MLL gene. As a result of these alterations, DOT1L is misregulated and causes inappropriate methylation, resulting in the increased expression of genes causing leukemia. Additional information about this program, including clinical trial information, may be found here: <http://clinicaltrials.gov/show/NCT01684150>.

Epizyme retains all U.S. rights to EPZ-5676 and has granted Celgene an exclusive license to EPZ-5676 outside of the United States. Epizyme has partnered with Abbott to develop a companion diagnostic to identify MLL-r patients. Additional information about these partnerships may be found here: [www.epizyme.com/about-us/partnerships/](http://www.epizyme.com/about-us/partnerships/).

### **Conference Call Information**

Epizyme will host a conference call and live audio webcast today at 8:30 a.m. ET to discuss initial findings from the dose escalation stage of the ongoing Phase 1 study. To participate in the conference call, please dial 1-877-844-6886 (domestic) or 1-970-315-0315 (international) and refer to conference ID 10332364. The live webcast and accompanying slides that provide additional detail about the dose escalation stage of this study can be accessed under "Upcoming Events" in the Investor Center section of the Company's website at [www.epizyme.com](http://www.epizyme.com).

The archived webcast will be available on the Company's website beginning approximately 2 hours after the live conference call.

### **About Epizyme, Inc.**

Epizyme, Inc. is a clinical stage biopharmaceutical company creating personalized therapeutics for patients with genetically defined cancers. Epizyme has built a proprietary product platform that the company uses to create small molecule inhibitors of a 96-member class of enzymes known as histone methyltransferases, or HMTs. HMTs are part of the system of gene regulation, referred to as epigenetics, that controls gene expression. Genetic alterations can result in changes to the activity of HMTs, making them oncogenic (cancer-causing). By focusing on the genetic drivers of cancers, Epizyme's targeted science seeks to match the right medicines with the right patients for a personalized approach to cancer treatment.

For more information, visit [www.epizyme.com](http://www.epizyme.com) and connect with us on Twitter at [@EpizymeRx](https://twitter.com/EpizymeRx).

### **Cautionary Note on Forward-Looking Statements**

The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial such as the results of our Phase 1 clinical study of EPZ-5676 described in this release do not necessarily predict final results. The treatment effects observed in our Phase 1 clinical study of EPZ-5676 were achieved by only a small number of patients in an open-label setting, were not statistically significant, might not represent any clinical benefit and might not be achieved by any other patient treated with EPZ-5676.

Any statements in this press release about future expectations, plans and prospects for the Company, including statements about the Company's strategy, future operations, clinical development of the Company's therapeutic candidates, expectations regarding the sufficiency of the Company's cash balance to fund operating expenses and capital expenditures, milestone or royalty payments from the Company's collaborators, the Company's anticipated milestones and future expectations and plans and prospects for the Company and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of

1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the uncertainties inherent in the initiation of future clinical trials, expectations of expanding ongoing clinical trials, availability and timing of data from ongoing clinical trials, expectations for regulatory approvals, development progress of the Company's companion diagnostics, availability of funding sufficient for the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements, other matters that could affect the availability or commercial potential of the Company's therapeutic candidates or companion diagnostics and other factors discussed in the "Risk Factors" section of the Company's 10-Q filed with the Securities and Exchange Commission on October 23, 2013. In addition, the forward-looking statements included in this press release represent the Company's views as of the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date hereof.

**Media/Investors:**

Jeff Boyle  
Epizyme, Inc.  
617.674.1778  
[jboyle@epizyme.com](mailto:jboyle@epizyme.com)

**Media:**

Luke Dickinson  
Spectrum  
202.955.6222 ext. 2503  
[ldickinson@spectrumspace.com](mailto:ldickinson@spectrumspace.com)

**Investors:**

Stephanie Ascher  
Stern Investor Relations  
212.362.1200  
[stephanie@sternir.com](mailto:stephanie@sternir.com)